February 9, 1948.

Dr. Jean Tavlitzki,
Institut de Biologie,
13 rue Pierre Curie,
Paris 5, France.

Dear Dr. Tavlitzki,

I am happy to answer your questions of your letter of the 26th.

The production of chloroacetate-resistant mutants which were also an-aerogenic was described by Penfold in 1911, but the glycolytic mechanism was too imperfectly understood then to allow of a precise specification of the metabolic deficiency. We understand now that the main source of gas in the coli fermentation of glucose is the splitting of formate, which is derived in turn from the phosphorolysis or hydrolysis of pyruvate.

The mutant and the parent (sensitive) were therefore tested on a series of substrates for their ability to produce gas. It was found that both strains were active on formate, but that the mutant had lost the capacity to produce H_2 from pyruvate. Both resting cells and growing cultures were used. It was concluded therefore that the metabolic deficiency was in the dismutation of pyruvate, which Lippman has shown ordinarily proceeds to acetyl-phosphate and formate. When a series of compounds were tested for their capacity to support growth when used as sole carbon source, it was noted that the mutant grew much more slowly on acetate than did the parent. To a lesser extent, the same was true of glycollate. Both mutant and parent grew well on pyruvate, lactate, the four-carbon acids, etc. When I resume work on this problem, which will be when my laboratory becomes more adequately equipped, I hope to test a larger selection of C_2 compounds and derivatives, since a C_2 derivative which can support the growth of the mutant may well represent "active acetate", about which there is so much discussion in relation to the initial condensation with oxalacetate in the Krebs cycle.

Penfold also noted that while the fermentation of glucose was anaerogenic, gas was produced from mannitol and other sugar alcohols. I have been able to confirm this, but have no verified opinions as to the immediate source of hydrogen in these cases.

A graduate student at Yale University, S.E. Reaume, has tried to produce correspomding mutants of yeast, but, I believe, found that chloroacetate was not inhibitory. I have noted the same thing on a variety of other (aerogenic) bacteria.

Yours sincerely,

Joshua Lederberg
Assistant Professor of Genetics.